**Package leaflet: Information for the user**
**Fluorouracil 25 mg/ml Solution for Injection or Infusion**

**Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

**What is in this leaflet**:



## 1. What Fluorouracil solution for injection or infusion is and what it is used for

Fluorouracil Solution for Injection or Infusion is an anti-cancer medicine. Treatment with an anti-cancer medicine is sometimes called cancer chemotherapy.

Fluorouracil Solution for Injection or Infusion is used to treat many common cancers, particularly cancers of the large bowel and breast. It may be used in combination with other anti-cancer medicines or radiotherapy.

You must talk to a doctor if you do not feel better or if you feel worse.

## 2. What you need to know before you use Fluorouracil solution for injection or infusion

**Do not use Fluorouracil Solution for Injection or Infusion**

- if you have shown signs of hypersensitivity (severe allergy) to fluorouracil or any of its ingredients in the past
- if you are in a seriously weakened state (including nutritional) due to long illness
- if you have a serious infection (e.g. chickenpox or shingles)
- if your bone marrow has been damaged by other cancer treatments (including radiotherapy)
- if you know that you do not have any activity of the enzyme dihydropyrimidine dehydrogenase (DPD) (complete DPD deficiency)
- if your cancer is non-malignant
- if you have serious liver disease
- if you have reduced activity/deficiency of the enzyme DPD (dihydropyrimidine dehydrogenase)
- if you are breast-feeding
- if you have been treated with brivudine, sorivudine or their chemically related analogues (antiviral drugs). Fluorouracil must not be taken within 4 weeks of treatment with brivudine, sorivudine or their chemically related analogues.

Tell your doctor if any of the above applies to you before this medicine is used.

**Warnings and precautions**

**Take special care with Fluorouracil Solution for Injection or Infusion**

- if your bone marrow is not producing blood cells normally (your doctor will do a blood test to check this)
- if you have any problems with your kidneys
- if you have any problems with your liver including jaundice (yellowing of the skin)
- if you have suffered from angina (chest pain) or have a history of heart disease, as you may be more likely to have an attack of angina or a heart attack, or show signs of heart problems when you take an ECG test
- if you have problems with your heart. Tell your doctor if you experience any chest pain during treatment
- if you are in generally poor health and have lost a lot of weight
- if you have had surgery within the last 30 days
- if you have had high dose radiation treatment to the pelvis
- if tumours have spread (metastasised) into your bone marrow
- if you have gastrointestinal (GI) side effects (oral ulceration (stomatitis), difficult to control vomiting, diarrhoea, dark sticky faeces containing partly digested blood, bleeding from the G.I. tract) or haemorrhage at any site
- if you know that you have a partial deficiency in the activity of the enzyme dihydropyrimidine dehydrogenase (DPD)
- if you have a family member who has partial or complete deficiency of the enzyme dihydropyrimidine dehydrogenase (DPD)

DPD deficiency: DPD deficiency is a genetic condition that is not usually associated with health problems unless you receive certain medicines. If you have DPD deficiency and take Fluorouracil injection, you are at an increased risk of severe side effects (listed under section 4 Possible side effects). It is recommended to test you for DPD deficiency before start of treatment. If you have no activity of the enzyme you should not take Fluorouracil injection. If you have a reduced enzyme activity (partial deficiency) your doctor might prescribe a reduced dose. If you have negative test results for DPD deficiency, severe and life-threatening side effects may still occur.

Contact your doctor immediately if you are concerned about any of the side effects or if you notice any additional side effects not listed in the leaflet (see section 4 Possible side effects).

Contact your healthcare provider immediately, if you experience the following signs or symptoms: new onset of confusion, disorientation, or otherwise altered mental status, difficulty with balance or coordination, visual disturbances. These could be signs of encephalopathy which can lead to coma and death, if left untreated.

Tell your doctor if any of the above applies to you before this medicine is used.

Fluorouracil can cause sensitivity to sunlight. This may result in increased skin reactions. To prevent this you must try to stay out of direct sunlight as much as possible while using it and must not use a sunlamp or sun bed.

Exposure to UV-radiation (e.g. natural sunlight, tanning salon) should be avoided.

Fluorouracil treatment may increase the likelihood of necrosis (death of tissue or skin) caused by radiation following radiotherapy.

The administration of fluorouracil has been associated with the occurrence of hand-foot syndrome, characterised as a tingling sensation of hands and feet, which may progress over a few days to pain when holding objects or walking. The palms and soles become swollen and tender.

**Other medicines and Fluorouracil**
Tell your doctor if you are taking, have recently taken or might take any other medicines.

Special care is needed if you are taking/using other medicines as some could interact with Fluorouracil Solution for Injection or Infusion, for example:

- Methotrexate, Cyclophosphamide, Cisplatin, Vinorelbine (anti-cancer medicines)
- Metronidazole (an antibiotic)
- Folinic acid (also called calcium folinate or calcium leucovorin - used to reduce the harmful effects of anti-cancer medicines)
- Interferon alfa (used in treatment of lymphomas and chronic hepatitis)
- Allopurinol (used to treat gout)
- Cimetidine (used to treat stomach ulcers)
- Warfarin (used to treat blood clots)
- Phenytoin (used to control epilepsy fits and also irregular heart rhythm)
- Radiation therapy
- Live vaccines should be avoided as these could cause serious or fatal infections. Contact should be avoided with people who have recently been treated with polio virus vaccine. Killed or inactivated vaccines may be administered; however, the response may be impaired.
- Sorivudine, brivudine or their chemically related analogues (anti-viral drugs)
- Tamoxifen (used in some types of breast cancer)
- Levamisol (used for treating infections with worms)
- Clozapine (used in some psychiatric disorders)

Fluorouracil treatment may interfere with some laboratory tests. Increases in total blood thyroxine concentration (due to increased binding to globulin) have been reported.

Please tell your doctor or pharmacist if you are taking or have recently taken these or any other medicines, including medicines obtained without a prescription.

**Pregnancy, breast-feeding and fertility**
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

Women must avoid becoming pregnant and use a highly effective method of contraception during treatment with Fluorouracil and for at least 6 months afterwards. Men treated with Fluorouracil are advised not to father a child during and for up to 3 months following the end of treatment.

Men and women should both seek advice on fertility such as conservation of eggs or sperm before treatment because of the possibility of irreversible infertility due to the therapy.

Fluorouracil should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

If pregnancy occurs during your treatment you must inform your doctor and should use genetic counselling.

Since it is not known whether fluorouracil passes into breast milk, breast-feeding must be discontinued before treatment with Fluorouracil Solution for Injection or Infusion.

Ask your doctor or pharmacist for advice before taking any medicine.

**Driving and using machines**
Do not drive or use machines if you experience any side effect (e.g. visual disturbance) which may lessen your ability to do so.

**Fluorouracil Solution for Injection or Infusion contains sodium**
The 10ml vial contains 40.1 mg of sodium (main component of cooking/table salt) in each vial. This is equivalent to 2% of the recommended maximum daily dietary intake of sodium for an adult.

The 20ml vial contains 80.2 mg of sodium (main component of cooking/table salt) in each vial. This is equivalent to 4% of the recommended maximum daily dietary intake of sodium for an adult.

The 100ml vial contains 401 mg of sodium (main component of cooking/table salt) in each vial. This is equivalent to 20% of the recommended maximum daily dietary intake of sodium for an adult.

## 3. How to use Fluorouracil solution for injection or infusion

This medicine is given into a vein or an artery. If it is given into a vein, it can either be injected (using a syringe) or infused (using a drip). If it is given into an artery, it will be given as an infusion.

If it is to be given as an infusion the medicine will be diluted before use.

**Recommended Dose**
Your doctor will work out the correct dose of Fluorouracil Solution for Injection or Infusion for you and how often it must be given.

The dose of medicine given to you will depend on your medical condition, your size, if you have had recent surgery and how well your bone marrow, liver and kidneys are working.

Your doctor will tell how well your bone marrow, liver and kidneys are working using blood tests.

The total daily dose should not exceed 1 gram.

There are no recommendations made regarding the use of Fluorouracil Solution for Injection or Infusion in children.

**If you use more Fluorouracil Solution for Injection or Infusion than you should**

This medicine will be given to you by a doctor or nurse. It is unlikely that you will be given too much or too little, however, tell your doctor or nurse if you have any concerns.

**If you forget to use Fluorouracil Solution for Injection or Infusion**

Do not take a double dose to make up for a forgotten dose.

## 4. Possible Side Effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

**If any of the following happen, tell your doctor immediately:**

- severe allergic reaction – you may experience a sudden itchy rash (hives), swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing), and you may feel you are going to faint
- chest pains
- shortness of breath
- your bowel motions are bloodstained or black
- your mouth becomes sore or develops ulcers
- numbness, tingling or tremor in the hands or feet
- heart attack or other heart problems such as quickening of your heart rate and breathlessness
- symptoms of leukoencephalopathy (disease of brain) – weakness, coordination problems in arms and legs; thinking/speech difficulties; vision/memory problems; seizures; headaches

These are very serious side effects. You may need urgent medical attention.

**If you experience any of the following tell your doctor as soon as possible:**

**Very common side effects (more than 1 in 10 patients):**

- Infections
- Sore throat
- Myelosuppression (a disorder in which the bone marrow produces reduced number of all types of blood cells [pancytopenia])
- Neutropenia and leukopenia (an abnormally low level of types of white blood cells in the blood)
- Thrombocytopenia (reduced numbers of platelets in the blood which reduces the ability of your blood to clot)
- A sharp drop in circulating granular white blood cells (agranulocytosis)
- Anaemia (condition in which your red blood cells are reduced)
- Wheezing (bronchospasm)
- Increased risk of infection due to immunosuppression
- Increase in uric acid in the blood
- Insufficient supply of blood to the heart which shows on the heart trace (ECG)
- Inflammation of the mucous lining of any of the structures in the mouth, throat and the digestive tract e.g. oesophagus (the gullet), rectum or anus
- Loss of appetite
- Watery diarrhoea
- Nausea
- Vomiting
- Hair loss
- Delayed wound healing
- Hand-foot syndrome (toxic skin reaction with redness and swelling of your hands and feet)
- Bleeding from the nose
- Fatigue, tiredness and lack of energy

- General weakness
- Liver cell damage

**Common side effects (less than 1 in 10 patients):**

- Infection in the blood stream (sepsis)
- Low white blood cells accompanied by fever
- Heart attack, angina pectoris (severe pain in the chest associated with an insufficient supply of blood to the heart)
- Changes in ECG (electrocardiogram- tests to check heart's rhythm and electrical activity)

**Uncommon side effects (less than 1 in 100 patients):**

- Dehydration
- Euphoria
- Rhythmic motions of the eyes (nystagmus) and disturbance of eye movement
- Headache
- Dizziness
- Symptoms of Parkinson’s disease (a progressive movement disorder marked by tremors, rigidity, slow movements)
- Pyramidal signs
- Sleepiness
- Excessive tear secretion or blocked tear ducts
- Blurred vision
- Eye movement disturbance
- Optic neuritis (a vision disorder characterised by inflammation of the optic nerve)
- Double vision
- Decrease in visual sharpness
- Excessive eye sensitivity to light and the aversion to sunlight or well lit places
- Red eyes (conjunctivitis)
- Inflammation of the eyelid margins (blepharitis)
- Lower eyelid turns outwards (ectropion)
- Narrowing of the duct which drains tears away from the eye (dacryostenosis)
- Abnormality in the heart’s rhythm
- Heart insufficiency or myocardial ischemia (reduced oxygen to the heart)
- Myocarditis (inflammatory disease of the heart muscle)
- Dilated cardiomyopathy (a type of heart disease in which the heart muscle is abnormally enlarged, thickened and/ or stiffened)
- Cardiac shock
- Low blood pressure
- Gastrointestinal ulceration and bleeding
- Casting off the skin
- Inflammation of the skin (dermatitis)
- Skin alterations e.g. dry skin, fissure erosion, redness of the skin, pruritic maculopapulor rash (an itchy, red bumpy rash)
- A skin eruption accompanying certain infectious diseases
- Appearance of itchy weals on the skin
- Skin sensitivity to light (photosensitivity)
- Increased pigmentation of the skin
- Streaky hyperpigmentation or depigmentation near the veins

- Changes in the nails (e.g. diffuse superficial blue pigmentation, hyperpigmentation; nail dystrophy, pain and thickening of the nail bed)
- Paronychia (inflammation of the tissue surrounding a fingernail)
- An inflammation of the matrix of the nail with formation of pus and shedding of the nail
- Sperm or ovum production disorder
- Sensations of imbalance and unsteadiness

**Rare side effects (more than 1 in 10,000 but less than 1 in 1,000 patients):**

- Generalised allergic reaction
- Severe, whole-body allergic reaction (anaphylaxis)
- Thyroid function changes - increase of T4 and T3 (total thyroxine and triiodothyronine)
- Mental confusion or impaired awareness especially regarding time, place or identity
- Insufficient blood flow in brain, intestine and limbs
- Poor blood circulation which makes the fingers and toes numb and pale (Raynaud's syndrome)
- Development of a clot within blood vessels
- Swelling (inflammation) of a vein caused by a blood clot
- Confusion

**Very rare side effects (less than 1 in 10,000 patients):**

- Symptoms of leukoencephalopathy (diseases affecting the white substance of the brain) including ataxia (loss of the ability to coordinate muscular movement)
- Cardiac arrest (sudden cessation of heartbeat and cardiac function)
- Sudden cardiac death (unexpected death due to heart problems)
- Damage of liver cells (cases with fatal outcome)
- Acute cerebellar syndrome
- Convulsion or coma in patients receiving high doses of 5-fluorouracil and in patients with dihydropyrimidine dehydrogenase (DPD) deficiency
- Bile or bile duct hardening
- Inflammation of the gall bladder
- Difficulty in articulating words
- Partial or total loss of the ability to communicate verbally or using written words
- Kidney failure
- Abnormal muscular weakness or fatigue

**Not Known (Frequency cannot be estimated from the available data):**

- Blood poisoning (septic shock)
- Neutropenic sepsis (a life-threatening reaction to an infection, which can happen in patients with neutropenia - low levels of a type of white blood cell that work as part of the immune system to fight infection in the blood)
- Lung infection
- Superinfection
- Urinary tract infection, bacterial infection of the urinary system
- Administration device related infection
- Bacterial infection of the skin causing redness, swelling and pain in the infected area
- Reduction in number of granulocytes, a type of white blood cell
- Undesirable immune system reactions (hypersensitivity)

- Reduced appetite
- Disorientation
- Numbness or weakness of the arms and legs
- Fits
- Hyperammonaemic encephalopathy (brain dysfunction caused by elevated ammonia)
- Cerebellar syndrome (uncontrolled movements including speech as a result of damage part of the brain)
- Clots in the heart chambers that could break off and block arteries in the body, which, for example, could cause a stroke or lack of blood supply to a limb
- Heart failure
- Inflammation of the heart muscle
- Condition characterised by headache, confusion, seizures and changes in vision (posterior reversible encephalopathy syndrome [PRES])
- Heart disease that presents with chest pain, shortness of breath, dizziness, fainting, irregular heartbeat (stress cardiomyopathy)
- Bleeding
- Dark sticky feces containing partly digested blood
- Drug-induced lupus erythematosus, which may cause fever, tiredness, joint and muscle pain, and rashes
- Fever
- Chest pain
- Injection site reaction
- Heart problems that can cause quickening of your heart rate and breathlessness
- Inflammation of the skin causing red scaly patches and possibly occurring together with pain in the joints and fever (cutaneous lupus erythematosus [CLE])
- Air in the intestinal wall
- Serious condition that presents with difficulty breathing, vomiting and abdominal pain with muscle cramps (lactic acidosis)
- Serious complication with rapid break down of cancer cells causing high levels of uric acid, potassium and phosphate (tumour lysis syndrome).

**Reporting of side effects**
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance. Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

Fluorouracil may lead to changes in your blood cells. Your doctor will take blood samples to check for these.

**If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.**

## 5. How to Store Fluorouracil Solution for Injection or Infusion

Keep this medicine out of the sight and reach of children.

**Expiry**
This medicine must not be used after the expiry date which is stated on the vial label and carton after 'EXP'. Where only a month and year is stated, the expiry date refers to the last day of that month.

**Storage**
Do not store above 25°C. Do not refrigerate or freeze. Keep the vials in the outer carton in order to protect from light.
Prepared infusions should be used immediately, however, if this is not possible they should not usually be stored for more than 24 hours at 2 – 8°C.

**Visible signs of deterioration**
Do not use this medicine if it appears brown or dark yellow in colour, or if particles are visible.

**Disposal**
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

## 6. Contents of the pack and other information

**What Fluorouracil Solution for Injection or Infusion contains**
The active substance is fluorouracil. Each millilitre (ml) of solution contains 25 mg of fluorouracil.

The other ingredients are sodium hydroxide (see section 2 "Fluorouracil Solution for Injection or Infusion contains sodium") and Water for Injections.

**What Fluorouracil Solution for Injection or Infusion looks like and contents of the pack**
Fluorouracil Solution for Injection or Infusion is a clear, colourless or slightly yellow solution for injection without visible particles, which comes in glass containers called vials.

It may be supplied in packs containing:
- 5 x 250 mg/10 ml vials
- 10 x 500 mg/20 ml vials
- 1 or 10 x 2.5 g/100 ml vial

Not all packs may be marketed.

**Marketing Authorisation Holder:**

Pfizer Healthcare Ireland
9 Riverwalk, National Digital Park
Citywest Business Campus
Dublin 24, Ireland

**Manufacturer Responsible for Batch Release in Europe:**
Pfizer Service Company BV, Hoge Wei 10, 1930 Zaventem, Belgium

**Manufacturer:**
Hospira Australia Pty Ltd, 1-5, 7-23 and 25-39 Lexia Place, Mulgrave, VIC 3170, Australia

**This leaflet was last revised in 12/2023.**

Ref: gxFU 16_0
---

**Fluorouracil 25 mg/ml Solution for Injection or Infusion**

**The following information is intended for medical or healthcare professionals only**

Further to the information included in section 3, practical information on the preparation/handling of the medicinal product is provided here.

**Incompatibilities**
Fluorouracil Solution for Injection or Infusion is incompatible with carboplatin, cisplatin, cytarabine, diazepam, doxorubicin, other anthracyclines and possibly methotrexate.

Formulated solutions are alkaline and it is recommended that admixture with acidic drugs or preparations should be avoided.

**Use and handling, and disposal**
The pH of Fluorouracil Solution for Injection or Infusion is 8.9 and the drug has maximal stability over the pH range 8.6 to 9.0.

If a precipitate has formed as a result of exposure to low temperatures, re-dissolve by heating to 60°C accompanied by vigorous shaking. Allow to cool to body temperature prior to use.

The product should be discarded if it appears brown or dark yellow in colour or if particles are visible.

Fluorouracil Solution for Injection or Infusion may be diluted with Glucose 5% Injection or Sodium Chloride 0.9% Injection or Water for Injections immediately before use.

Chemical and physical in-use stability has been demonstrated for 5 days at 20-21°C. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would not normally be longer than 24 hours at 2-8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

Cytotoxic Handling Guidelines
Should be administered only by, or under the direct supervision of, a qualified physician who is experienced in the use of cancer chemotherapeutic agents.

Fluorouracil Solution for Injection or Infusion should only be prepared for administration by professionals who have been trained in the safe use of the preparation. Preparation should only be carried out in an aseptic cabinet or suite dedicated for the assembly of cytotoxics.

In the event of spillage, operators should put on gloves, face mask, eye protection and disposable apron and mop up the spilled material with an absorbent material kept in the area for that purpose. The area should then be cleaned and all contaminated material transferred to a cytotoxic spillage bag or bin and sealed for incineration.

*Contamination*
Fluorouracil is an irritant, contact with skin and mucous membranes should be avoided.

In the event of contact with the skin or eyes, the affected area should be washed with copious amounts of water or normal saline. A bland cream may be used to treat the transient stinging of the skin. Medical advice should be sought if the eyes are affected or if the preparation is inhaled or ingested.

Please refer to the marketing authorisation holder for COSHH hazard datasheets.

*Preparation Guidelines*

a) Chemotherapeutic agents should be prepared for administration only by professionals who have been trained in the safe use of the preparation.
b) Operations such as reconstitution of powder and transfer to syringes should be carried out only under aseptic conditions in a suite or cabinet dedicated for the assembly of cytotoxics.
c) The personnel carrying out these procedures should be adequately protected with clothing, gloves and eye shield.
d) Pregnant personnel are advised not to handle chemotherapeutic agents.

*Disposal*

Syringes containing remaining solution, absorbent materials, and any other contaminated material should be placed in a thick plastic bag or other impervious container and incinerated at 700°C.